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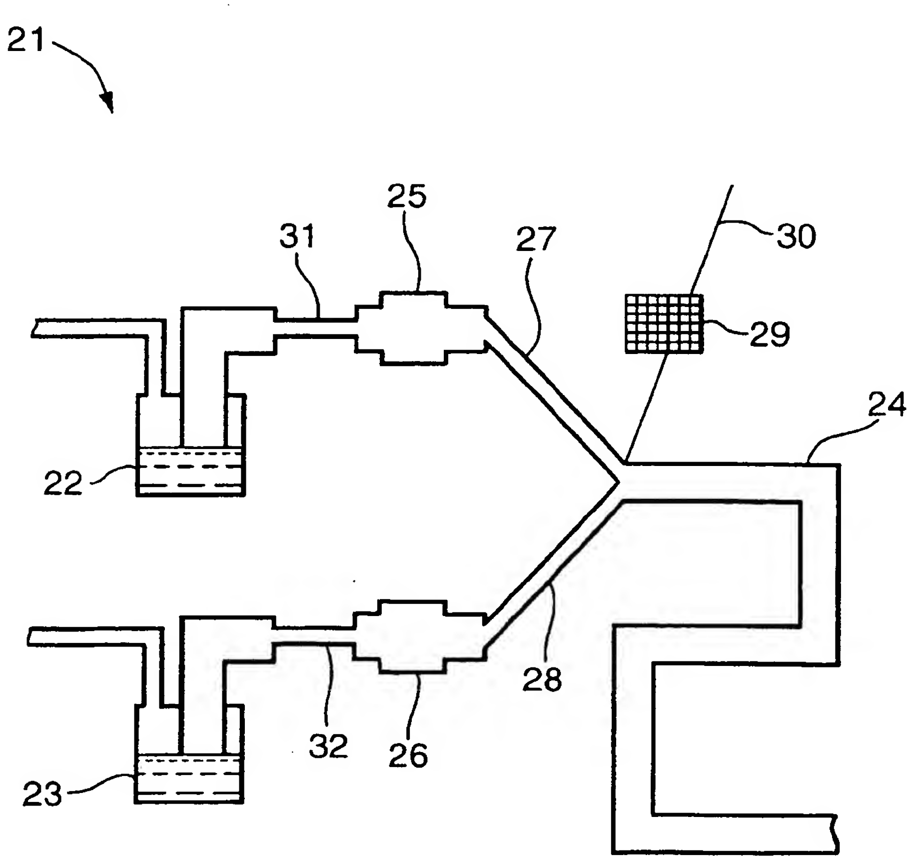
(54) Title: MICROCHANNEL DEVICE



(57) Abstract: This invention relates to a microchannel device comprising a microchannel and a liquid introduction means for introducing at least two liquids into the microchannel; characterised in that the introduction means comprises a pulse means for introducing each liquid into the microchannel in the form of a plurality of pulses, and for staggering the pulses of each liquid relative to the pulses of the other liquids. The device may be used to mix liquids for microfluidic applications.

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Microchannel device

This invention relates to a new microchannel device. More particularly this invention relates to a new microchannel device that facilitates the mixing of two or more fluids in a microchannel. This invention also relates to a new method of mixing together two or more fluids in a microchannel.

A microchannel device is one that has one or more microchannels along which a fluid may flow, the microchannel or each microchannel having a dimension, perpendicular to the channel, between 100 nm and 1 mm. In addition to a microchannel the device may comprise other components such as: a chamber, a filter, an electrode, a pump, a valve, or a mixing system. Microchannels may be formed from PTFE, plastic, glass, quartz, or by micromachining a silicon wafer.

Microchannel devices are used for analytical and synthetic applications that involve very small quantities of substances. For example the reagents used for an analytical process may be expensive; by performing the process in a microchannel device the quantities of chemical required are small and hence the cost is minimised.

The combination of some chemicals, because of their highly reactive nature, may only be possible at a small scale.

Because microchannel devices may be mass produced at relatively low cost, a reaction can be scaled up simply by performing the reaction simultaneously in the required number of microchannel devices.

Performing reactions and other processes at such a small scale can, however, present some significant problems. A particular area of concern is the combination of two or more fluids, necessary as the first step in bringing about a chemical reaction. Because of laminar flow, it is usually insufficient simply to flow the two fluids together; the adjacent flow only resulting in the fluids remaining largely unmixed. This laminar flow results

from the small dimensions of the channels and the flow velocities conventionally used in microfluidics. Such mixing that does occur results from diffusion across the interface between the two fluids.

One way in which this problem may be addressed is by dividing the flow of each fluid to be mixed into multiple streams, each stream having a reduced cross-sectional area, as shown in figure 1.. Figure 1 is a schematic diagram of part of a prior art device by which multiple streams may be generated. A plurality of microchannels 11, 12, 13, 14, 15, and 16 are fabricated on a silicon chip 17. The microchannels 11 to 16 comprise a first microchannel 11, a second microchannel 12, a third microchannel 13, a fourth microchannel 14, a fifth microchannel 15, and a sixth microchannel 16. The first microchannel 11 contains a first fluid, and the second microchannel 12 contains a second fluid. The arrow 18 shows the direction in which both fluids flow. The first microchannel 11 flows into the third 13 and a fourth 14 microchannel, both of reduced dimension perpendicular to the flow. The second microchannel 12 flows into a fifth 15 and sixth 16 microchannel, also both of reduced cross-sectional dimension perpendicular to the flow. The fourth 14 and fifth 15 microchannels are fabricated in such a manner that they cross but do not intersect.

As a result of crossing of the fourth 14 and fifth 15 microchannels a spatially alternating order of fluids is obtained. The order of the fluids at the bottom of figure 1, from right to left, is: first fluid, second fluid, first fluid, and second fluid. The four streams contained in the third 13, fourth 14, fifth 15, and sixth 16 microchannels may be combined into a single microchannel (not shown in figure 1) in such a manner that the alternating order and reduced cross-sectional area is retained. In this way interaction and therefore mixing by diffusion is enhanced.

The figure 1 apparatus represents a less than ideal solution since it is relatively complex and difficult to fabricate. In particular, it is difficult to micromachine channels that cross but do not intersect. A further problem with the figure 1 apparatus is that it is difficult to alter the ratio of the first

and second liquids in the resulting mixture, the ratio being largely decided by the relative cross-sectional areas of the microchannels.

A second way in which two fluids flowing in a microchannel may be combined is by simply increasing the flow rate through the microchannels until the Reynolds numbers are greater than approximately 2300. For such high Reynolds numbers there is turbulent flow and consequent mixing of the fluids. For pressure driven flow, in order to obtain sufficiently high flow rates for Reynolds numbers greater than 2300, pressures in excess of 1 million Pa may be required. This will necessitate the use of relatively robust microchannel devices, which in practice may be difficult to fabricate.

The following prior art is considered to be relevant to the present invention. GB 2355414 A describes a micro-mixer having opposed nozzles. DE 196 11 270 A1 describes a micro-mixer for very small volumes of liquid. US 6,150,119 describes the serial introduction of multiple different samples into a microfluidic channel network.

Further relevant prior art was presented, by A. Deshmukh, at the Solid State Sensors and Actuator Workshop, June 4-8, 2000, Crowne Plaza Resort, Hilton Head, South Carolina, USA.

It is an object of the present invention to provide a new microchannel device, and a new method of mixing two or more fluids in a microchannel, that reduces the above mentioned problems.

According to a first aspect, the invention provides a method of mixing at least two fluids in a microchannel, comprising the steps: (a) introducing each fluid into the microchannel, and (b) flowing each fluid along the microchannel; wherein the step (a) comprises the steps of (i) introducing each fluid into the microchannel in the form of a plurality of pulses, and (ii) staggering said plurality of pulses, of each fluid, relative to those of the other fluid or fluids.

For the purposes of this specification a fluid is to be taken as any substance that is either a liquid or a gas. For the absence of doubt, the term "liquid" should be taken to include solutions and suspensions.

Preferably each of the fluids, to be mixed by the method of mixing according to the invention, is a liquid.

The pulses may be formed by repeatedly increasing and decreasing the rate at which each fluid is introduced into the microchannel. The pulses may be formed by repeatedly stopping and starting the flow of each fluid into the microchannel. For example the pulses may be formed by repeatedly opening and closing a valve. Alternatively the pulses may be formed by modulation of the introduction of each fluid by means of a controllable pump. The formation of a pulse need not involve the complete cessation of fluid flow into the microchannel for any of the components to be mixed.

Staggering may be achieved by sequentially opening and closing a plurality of valves. By staggering the pulses, different fluids may be introduced at different times. For example only one of the fluids may be introduced at a given time, by ensuring that one valve is open while the other valve or valves are closed.

Staggering the pulses causes the fluids to mix more efficiently in the microchannel. The efficiency of the technique means that the utilisation of high pressures and complex structures is not required. The reason for this improvement in mixing is due to some degree of spatial separation between the different fluids along the length of the microchannel and normal to it. A further factor is the non-uniform flow profile across the width of the microchannel, the flow being fastest at the centre of the microchannel. The combination of these two factors results in an increased interfacial area between adjacent pulses as they proceed along the channel, and to a reduced mean diffusion path required for mixing between the pulses by virtue of their thinning as the interfacial area increases.

By contrast, prior art methods often tend to result in spatial separation of the different fluids across the width of the microchannel. For this case, the non-uniform flow profile will not promote mixing.

For the present invention it may be that the spatial separation along the length, as opposed to the width, of the microchannel allows flow along the microchannel to cause mixing of the different fluids. It should be noted that any spatial separation between the components, along the length of the microchannel, is likely to be most pronounced in the region of the microchannel at which the fluids are introduced. Such spatial separation tending to diminish as the fluids pass along the microchannel due to the non-uniform flow across the microchannel.

Each pulse may be introduced into the microchannel in such a manner that it is in contact with opposite sides of the microchannel.

The duration between any one of the valves being open and being closed may be less than 5 seconds. The duration between any one of the valves being closed and being open may be less than 0.1 seconds. A delay may be introduced between the opening of one valve and the closing of another, such a delay may be less than 0.1 seconds.

Each fluid may be introduced into the microchannel at substantially the same position in the microchannel as the other fluids.

Preferably each of the fluids may be introduced into a portion of the microchannel, of width w, the portion having a length of less than 5w, measured along the direction of flow of the fluids in the microchannel. More preferably each of the fluids may be introduced into a portion of the microchannel, the portion having a length of less than 2w.

Advantageously step (a) is performed in such a manner that the flow of each of the fluids, upon entry into the microchannel, is substantially

perpendicular to the length of the microchannel.

Step (a) may be performed by introducing each fluid into the microchannel through at least one inlet channel.

The microchannel may be attached to or formed in a substrate. For the purposes of this specification the term "depth of the microchannel" shall be defined as the cross-sectional dimension of the microchannel that is substantially perpendicular to the plane of the substrate; and the term "depth of the inlet channel" shall be defined as the cross-sectional dimension of the inlet channel, at the point of entry of the inlet channel into the microchannel, that is substantially perpendicular to the plane of the substrate.

The depth of the or at least one of the inlet channels may be less than the depth of the microchannel.

The depth of the or at least one of the inlet channels may be less than one half of the depth of the microchannel.

The depth of the or at least one of the inlet channels may be less than one tenth of the depth of the microchannel.

The cross-sectional area of the or at least one of the inlet channels may be less than the cross-sectional area of the microchannel.

The cross-sectional area of the or at least one of the inlet channels may be less than half of the cross-sectional area of the microchannel.

The cross-sectional area of the or at least one of the inlet channels may be less than one tenth of the cross-sectional area of the microchannel.

Preferably the volume of the microchannel is less than 20 μl. More preferably the volume of the microchannel is less than 5 μl.

Advantageously step (a) is performed in such a manner that at least one of the pulses of one fluid contacts the pulse of another fluid as it enters the microchannel.

The location, pressure, and time at which each fluid is introduced may be such that vortices are established in the microchannel as a result of interaction between the or at least two of the fluids.

The formation of vortices by the introduction of fluids into the microchannel may assist in mixing the fluids together.

The microchannel may have at least one cross sectional dimension less than 100 µm. The microchannel may have a cross-sectional area less than 10,000 µm^2.

The introduction of the or at least two of the fluids into the microchannel may be performed in such a manner that the flow of fluid at the end of the microchannel, remote from the region in which the fluids are introduced, may be substantially continuous for a period greater than 100 seconds.

Many synthetic and analytical techniques require a relatively constant flow of reactant or product, a criterion that may be met by this invention. For example continuous operation of valves introducing the fluids allows continuous output from the microchannel.

The composition of the resulting mixture may be altered by altering the relative duration of the pulses. For example if a first fluid is to be mixed with a second fluid, then the proportion of the first fluid can be increased by increasing the pulse length of the first fluid relative to that of the second.

Again this is a significant feature with regard to many synthetic and analytical applications, which require variation in the proportion of a

reactant for a given mixture.

In the case in which two fluids are to be mixed, high ratios, for example 10:1, 100:1, and 1000:1, of mixing may be achieved

Preferably the formation and staggering of the pulses is performed in such a manner that only one fluid is introduced into the microchannel at any given time. More preferably the formation and staggering of the pulses is performed in such a manner that the fluid being introduced into the microchannel is repeatedly altered.

Advantageously the method comprises the further step of using an electronic component to control the duration of each pulse. More preferably the electronic component comprises a computer.

Advantageously the dimensions of the microchannel and the rate at which the fluids are introduced into the microchannel is such that the flow of fluid through the microchannel is non-uniform across the width of the microchannel. More advantageously the flow of fluid through the microchannel is substantially parabolic. In other words the velocity distribution, across at least one line of cross-section, is substantially parabolic. It is believed that this parabolic flow results in greater interaction between the different components to be mixed, enhancing the area of interaction, reducing spatial separation, and therefore the distance required for diffusion to effect mixing as the pulses flow along the microchannel.

Preferably the flow of each of the fluids through the microchannel is caused only by introduction of each of the fluids into the microchannel. In other words the flow of each of the fluids through the microchannel is not caused by introduction of gas into the microchannel. Gas may be used to apply pressure to the fluids to be mixed, provided contact between the gas and the fluid does not occur within the microchannel. Alternatively, flow may be induced by a microfluidic pump or by an electrokinetic phenomenon.

Step (b) may comprise the step of electrokinetically pumping at least some of the fluids in the microchannel. Step (b) may comprise the step of electrokinetically pumping at least some of the fluids in the microchannel in such a manner that parabolic flow is induced.

If the fluids to be mixed are liquids, then the flow of each of the liquids through the microchannel without the use of gas in the microchannel minimises the risk of contamination, either by dissolution of the gas in the liquid, or bubble formation.

Advantageously step (a) comprises the step of introducing each fluid into the microchannel by means of an electrokinetic pump.

Preferably step (a) is performed in such a manner that each pulse contacts part of the microchannel wall substantially opposite the inlet channel through which it was introduced.

By performing step (a) in this manner, it is possible to form a pulse that is in contact with the region of the inlet channel and in contact with the region of the microchannel wall opposite to the inlet channel. The flow along the channel of a pulse at the opposite points of contact will be inhibited relative to the flow along the channel at the points along the line joining the opposite points of contact. It is believed that the difference in flow rates between the middle of a pulse and the edges of a pulse benefits the mixing process.

Step (a) may comprise the step of causing each pulse to contact two points in said microchannel in such a manner that a line between said contact points is substantially perpendicular to the direction of fluid flow through the microchannel.

Advantageously each pulse is introduced through at least two inlet channels. More advantageously the two or two of the inlet channels, through which each pulse is introduced, are located substantially opposite

each other.

The fluid from the two or more inlet channels flows together in the microchannel to form each pulse. The formation of each pulse by the flow of fluid through two or more inlet channels allows each pulse to contact the microchannel at points, in the region of the inlets through which the pulse was introduced that are spaced from one another. Flow of each pulse is inhibited at the points of contact, assisting the mixing process.

Step (b) may comprise the step of applying gas pressure to the fluid in the microchannel by means of a hydrophobic membrane.

According to a second aspect the invention provides a microchannel device comprising a microchannel and a fluid introduction means for introducing at least two fluids into the microchannel; characterised in that the introduction means comprises a pulse means for introducing each fluid into the microchannel in the form of a plurality of pulses, and for staggering the pulses of each fluid relative to the pulses of the other fluids.

Preferably the fluid introduction means comprises a liquid introduction means for introducing at least two liquids into the microchannel; and the liquid introduction means comprises a pulse means for introducing each liquid into the microchannel in the form of a plurality of pulses, and for staggering the pulses of each liquid relative to the pulses of the other liquids.

Advantageously the fluid introduction means comprises at least one inlet channel each pulse being introduced into the microchannel through the or at least one of the inlet channels, the or each inlet channel having an inlet opening formed in the wall of the microchannel.

Each inlet channel may be substantially perpendicular to the microchannel.

The introduction means may comprise a valve, associated with one of the

fluids; the valve, microchannel, and fluid being arranged such that opening and then closing the valve causes a pulse of fluid to be released into the microchannel.

Preferably the introduction means comprises a plurality of valves. More preferably the control means comprises a means for sequentially opening and closing each of said plurality of valves. Yet more preferably the control means comprises a means of opening only one valve at any given time and for ensuring that the other valve or valves are closed. Even more preferably the control means comprises a means for repeatedly altering which of said plurality of valves is open at any given time.

The control means may comprise a means for forming said plurality of pulses by repeatedly stopping and starting the flow of fluid into the microchannel.

The introduction means may comprise an electrokinetic pump, associated with one of the fluids; the electrokinetic pump, microchannel, and fluid being arranged such that the activation of the electrokinetic pump causes a pulse of fluid to be released into the microchannel. The electrokinetic pump may be arranged and activated in such a manner that a non uniform velocity profile is generated across the microchannel. The electrokinetic pump may be arranged and activated in such a manner that a parabolic velocity profile is generated across the microchannel.

Preferably the introduction means comprises a plurality of electrokinetic pumps. More preferably the control means comprises a means for sequentially activating and deactivating each of said electrokinetic pumps. Yet more preferably the control means comprises a means of activating only one electrokinetic pump at any given time and for ensuring that the other electrokinetic pump or pumps are inactive. Even more preferably the control means comprises a means for repeatedly altering which of said plurality of electrokinetic pumps is activated at any given time.

The means for introducing each fluid into the microchannel in the form of a plurality of pulses may have a construction such that each pulse is in contact with opposite sides of the microchannel.

Each valve may be connected, by means of an inlet channel, to the microchannel.

Preferably each said inlet opening may be formed within a portion of the microchannel having a length less than 10 mm. More preferably each said inlet opening may be formed within a portion of the microchannel having a length less than 5 mm.

Advantageously the pulse means is constructed in such a manner that the flow of each of the fluids into the microchannel is substantially perpendicular to the length of the microchannel.

The depth of each inlet channel may be less than the depth of the microchannel.

The depth of each inlet channel may be less than half of the depth of the microchannel.

The depth of each inlet channel may be less than one tenth of the depth of the microchannel.

The cross-sectional area of each inlet channel may be less than the cross-sectional area of the microchannel.

The cross-sectional area of each inlet channel may be less than one half of the cross-sectional area of the microchannel.

The cross-sectional area of each inlet channel may be less than one tenth of the cross-sectional area of the microchannel.

The at least part of the fluid associated with each valve may be contained in a reservoir in such a manner that fluid may flow from the reservoir into the valve.

Preferably the microchannel has a smallest cross-sectional dimension between 500 μm and 100 nm. More preferably the microchannel has a smallest cross-sectional dimension between 100 μm and 1 μm.

The microchannel may comprise at least two sub-channels, each sub-channel being substantially parallel to the microchannel, the cross-sectional area of each sub-channel being less than that of the microchannel, and each sub-channel being located within the microchannel.

Provided that each sub-channel is sufficiently long parabolic flow may be established in each sub-channel. The establishment of parabolic flow in each sub-channel assists the mixing process.

Advantageously the control means comprises a means for allowing only one of the fluids to be introduced into the microchannel at any given time. More advantageously the control means comprises a means for repeatedly altering which of the fluids is to be introduced into the microchannel.

Preferably control means comprises an electronic component. More advantageously the control means comprises a computer. Yet more advantageously the control means comprises a computer that has been programmed to operate in real time.

Advantageously the fluid introduction means has a construction such that each pulse is introduced through one inlet channel, and such that each pulse contacts part of the microchannel wall substantially opposite the inlet channel through which it was introduced.

Preferably the fluid introduction means has a construction such that each

pulse is introduced through at least two inlet channels. More preferably the fluid introduction means has a construction such that each pulse is introduced through two inlet channels disposed on opposite sides of the microchannel.

Advantageously the microchannel is substantially closed at one end. More advantageously the microchannel is closed at the end of the microchannel that is substantially adjacent to at the or at least one of the inlet channels.

According to a third aspect the invention provides a method of mixing at least two fluids in a microchannel, comprising the step of introducing each of the fluids into the microchannel in such a manner that there is at least some spatial separation between the fluids along the length of the microchannel; characterised in that the method comprises the further step of propelling each fluid, located in the microchannel, along the microchannel in such a manner that substantially parabolic flow occurs in at least part of each fluid located in the microchannel.

According to a fourth aspect the invention provides a microchannel device comprising a microchannel and a fluid introduction means for introducing at least two fluids into the microchannel in such a manner that there is at least some spatial separation between the fluids along the length of the microchannel; characterised in that the microchannel device further comprises a propelling means for propelling each fluid, located in the microchannel, along the microchannel in such a manner that substantially parabolic flow occurs in at least part of the fluids located in the microchannel.

The invention will now be described, by way of example only, with reference to figures 2 and 3. The figures are:

Figure 1, which shows a schematic diagram of part of a prior art microchannel device;

Figure 2, which shows a schematic diagram of a microchannel device according to the invention;

Figure 3,. which shows a schematic diagram of a microchannel device, according to the invention, comprising at least two sub-channels;

Figure 4, which shows a schematic diagram of a microchanel device, according to the invention, in which each pulse of liquid is introduced through two inlet channels;

Figure 5 shows a schematic diagram of a microchannel device according to the invention, in which each inlet channel is perpendicular to the microchannel;

Figure 6 shows the absorption of light by a microchannel device, according to the invention, containing two fluids, as a function of the distance along the microchannel; and

Figure 7 shows modelling results relating to injection of pulses into a microchannel by a method according to the present invention.

Figure 2 shows a schematic diagram of a microchannel device according to the invention generally indicated by 21. First and second reservoirs 22, 23 are connected to a microchannel 24 via first and second valves 25, 26 and flow restrictors 27, 28, 31 and 32. The first reservoir 22 contains a first liquid and the second reservoir 23 contains a second liquid. For the purposes of this example the first liquid will be taken to be an aqueous solution of a first water soluble dye, and the second liquid will be taken to be an aqueous solution of a second water soluble dye.

The mixing microchannel 24 has cross sectional dimensions 1 mm x 100 microns. In other words the microchannel 24 has a width of 1 mm and a depth of 100 microns. The total length of the microchannel 24 is 19 cm and it is arranged in a serpentine structure to conserve space. The

microchannel 24 is fabricated by bonding together two laminae of polymethyl methacrylate (PMMA) by applying pressure at 120C. The microchannel structures are formed in one of the PMMA layers by micromilling. Connection conduits are formed through the other PMMA layer to allow connection to the buried microchannel structure. Metal tubes are glued into the connection conduits to allow easy connection of plastic tubing.

A pressure of 40 KPa is applied to the first and second liquids by means of compressed air. The input of the first and second liquids into the microchannel 24 is controlled by two valves 25 and 26. Gas pressure is therefore used to introduce the first and second liquids into the microchannel 24, but does not itself enter the microchannel 24.

The first and second valves 25, 26 are connected to a control means (not shown in figure 2) that controls whether the first and second valves 25, 26 are open or closed. The control means may be programmed so that only one of the first and second valves 25, 26 is open at any given time. The control means may also alternate which of the two valves 25, 26 is open so that alternating pulses of the first and second solutions are released into the microchannel 24. In this way the introduction of the first and second liquid is staggered so that the first liquid is not introduced at the same time as the second liquid.

The duration of each pulse, for either the first or the second liquids, is approximately 0.8 seconds. 1.2 pulses are released into the microchannel 24 per second. By staggering the pulses, some degree of spatial separation, between the first and second liquids, occurs along the length of the microchannel 24. This spatial separation is greatest in the region of the microchannel 24 at which the two liquids are introduced. As the two liquids move along the microchannel 24 they become mixed.

Valves 25 and 26 are commercially available solenoid valves. Each valve 25 and 26 displaces fluid when it closes, exerting a pumping action. The

pumping action can be minimised by locating flow restrictors 27, 28, 31, and 32 on both sides of each valve. Each flow restrictor has a length of 5 mm, a depth of 40 microns and width of 100 microns.

By having flow restrictors 27, 28, 31, and 32 placed on both sides of each valve, the effect of liquid flow in the microchannel of the closing action of the first and second valves 25, 26 is minimised. The closure of the first and second valves 25, 26 tends to cause an increase in pressure in the region of the valves 25, 26. The arrangement of the flow restrictors results in the microchannel being shielded from the pumping effect of the solenoid valves 25, 26.

In the figure 2 embodiment of the invention, the flow restrictors 27 and 28 form the inlet channels by which the first and second liquids are introduced into the microchannel. In other words the dimensions of the inlet channels, for the figure 2 embodiment are: 40 microns (depth), 100 microns (width), and 5 mm (length).

After a mixture of the first and second liquids has been delivered to the microchannel 24. The fluid contained in the microchannel 24 may be delivered by application of gas pressure to the fluid. Pressure is applied via a gas line 30, conveniently at a pressure of 10kPa, which is connected via a hydrophobic membrane 29 which allows passage of gas but not aqueous based liquids. Thus when fluid was delivered to the microchannel 24 via valves 25 and 26, flow is stopped by the hydrophobic membrane 29. The delivery of the fluid along the microchannel 24 in this way also causes a mixing action.

In a further embodiment, not shown in the figures, a microchannel device according to the invention may have an identical construction to that of the figure 2 device, save that it has a microchannel depth of 200 microns.

Figure 3 shows a microchannel device, generally indicated by 31, comprising a microchannel 32 and inlet channels 35, 36. The microchannel

comprises three sub-channels 33, formed by baffles 34. Liquids flow down the length of the microchannel 31 and undergo mixing. If the sub channels are sufficiently long then parabolic flow of the liquid through the sub-channel may occur. The presence of the baffles 34 therefore increases the mixing interaction between the liquids, relative to that which would have occurred in the absence of the baffles 34.

Figure 4 shows a microchannel device, generally indicated by 41, having first inlet channels 42, 43, and second inlet channels 44, 45. The inlet channels 42, 43, 44, and 45 form inlet openings 42a, 43a, 44a, and 45a in the wall of the microchannel 46. A first liquid is introduced through the first inlet channels 42 and 43, and a second liquid is introduced through the second inlet channels 44 and 45. The first and second liquids are introduced in the form of a plurality of pulses. Each pulse of the first liquid is formed by the substantially simultaneous flow of liquid through both the first inlet channels 42, 43. Each pulse of the second liquid is formed by the substantially simultaneous flow of liquid through both the second inlet channels 44, 45. The two first inlet channels 42, 43 are arranged on opposite sides of the microchannel, and the two second inlet channels 44, 45 are also arranged on opposite sides of the microchannel to each other. This arrangement of the inlet channels 42, 43, 44, and 45 causes greater interaction of the two liquids as they flow along the microchannel. Figure 5 shows a schematic diagram of a further microchannel device, generally indicated by 51, according to the invention. The microchannel device is identical to that shown in figure 3, save that it does not comprise sub channels. The cross sectional dimensions of the microchannel 52 are 1mm (width) by 200 microns (depth). The inlet channels 53 have cross sectional dimensions 100 microns (width) by 40 microns (depth). The inlet channels 53 are arranged so that they are perpendicular to the microchannel 52 , and the end of the microchannel 52 adjacent to the inlet channel 53 is closed. The walls of the figure 5 microchannel 52 are constructed from a transparent material.

Figure 6 shows the results of an experiment conducted using the figure 5

apparatus. Pulses of water and an aqueous solution of red dye are introduced into the figure 5 microchannel by a method according to the invention. The figure 6 plot shows the concentration, in the centre or the channel, of red dye in the microchannel versus distance along the microchannel. The concentration of the red dye in the microchannel is determined by measuring the absorption of light by the liquid in the channel. The concentration being determined by the Beer Lambert law. Figure 6 illustrates the mixing effectiveness of the methods and devices of the invention.

CFD (Flume CAD (RTM) (Conventor)) was used to investigate mixing of two fluids by a method according to the invention. The results of the 2D calculation are shown in figure 7(a). Figure 7(a) shows the injection of a pulse through one of the inlet channels 71. As can be seen from the figure 7(a) results, the pulse does not reach the opposite wall of the microchannel 72.

Figure 7(b) shows the results for the same microchannel device, as for figure 7(a). However, the figure 7(b) calculation was performed for a 3D simulation. The reason for the difference between the figure 7(a) and 7(b) results is that the figure 7(b) calculation takes account of the difference of the depths of the inlet channel 71 and microchannel 72. Because the figure 7(a) results are for a 2D calculation, the depth of the injection channel is effectively the same as the depth of the microchannel for these results. The figure 7 results therefore show that it is advantageous that the depth of each of the inlet channels should be less than the depth of the microchannel.

Claims

1. A method of mixing at least two liquids in a microchannel, comprising the steps: (a) introducing each liquid into the microchannel, and (b) flowing each liquid along the microchannel; wherein the step (a) comprises the steps of (i) introducing each liquid into the microchannel in the form of a plurality of pulses, and (ii) staggering said plurality of pulses, of each liquid, relative to those of the other liquid or liquids.

2. A method according to claim 1 wherein step (a) is performed in such a manner that each liquid is introduced into the microchannel at substantially the same position in the microchannel as the other liquids.

3. A method according to claim 1 wherein the location, pressure, and time at which each liquid is introduced is such that vortices are established in the microchannel as a result of interaction between the or at least two of the liquids.

4. A method according to claim 1 wherein step (a) is performed in such a manner that the flow of liquid at the end of the microchannel, remote from the region in which the liquids are introduced, may be substantially continuous for a period greater than 100 seconds.

5. A microchannel device comprising a microchannel and a liquid introduction means for introducing at least two liquids into the microchannel; characterised in that the introduction means comprises a pulse means for introducing each liquid into the microchannel in the form of a plurality of pulses, and for staggering the pulses of each liquid relative to the pulses of the other liquids.

6. A microchannel device according to claim 5 wherein the introduction means comprises a valve, associated with one of the liquids; the valve, microchannel, and liquid being arranged such that opening and then closing the valve causes a pulse of liquid to be released into the

microchannel.

7. A microchannel device according to claim 6 wherein the introduction means comprises a plurality of valves.

8. A microchannel device according to claim 5 wherein the liquid introduction means comprises at least one inlet channel, each pulse being introduced into the microchannel through the or at least one of the inlet channels, the or each inlet channel having an inlet opening formed in the wall of the microchannel.

9. A microchannel device according to claim 8 wherein each said inlet opening is formed within a portion of the microchannel having a length less than 10 mm.

10. A microchannel device according to any one of claims 5 to 9 wherein the microchannel has a smallest cross-sectional dimension between 1 mm and 100 nm.

11. A microchannel according to any one of claims 5 to 10 wherein the dimensions of the microchannel and the rate at which the liquids are introduced into the microchannel is such that the flow of liquid through the microchannel is substantially parabolic.

12. A microchannel device according to claim 8 wherein the depth of each inlet channel is less than the depth of the microchannel.

13. A microchannel device according to claim 12 wherein the depth of each inlet channel is less than half of the depth of the microchannel.

14. A microchannel device according to claim 5 wherein the microchannel comprises at least two sub-channels, each sub-channel being substantially parallel to the microchannel, the cross-sectional area of each sub-channel being less than that of the microchannel, and each sub-channel being

located within the microchannel.

Fig.1.

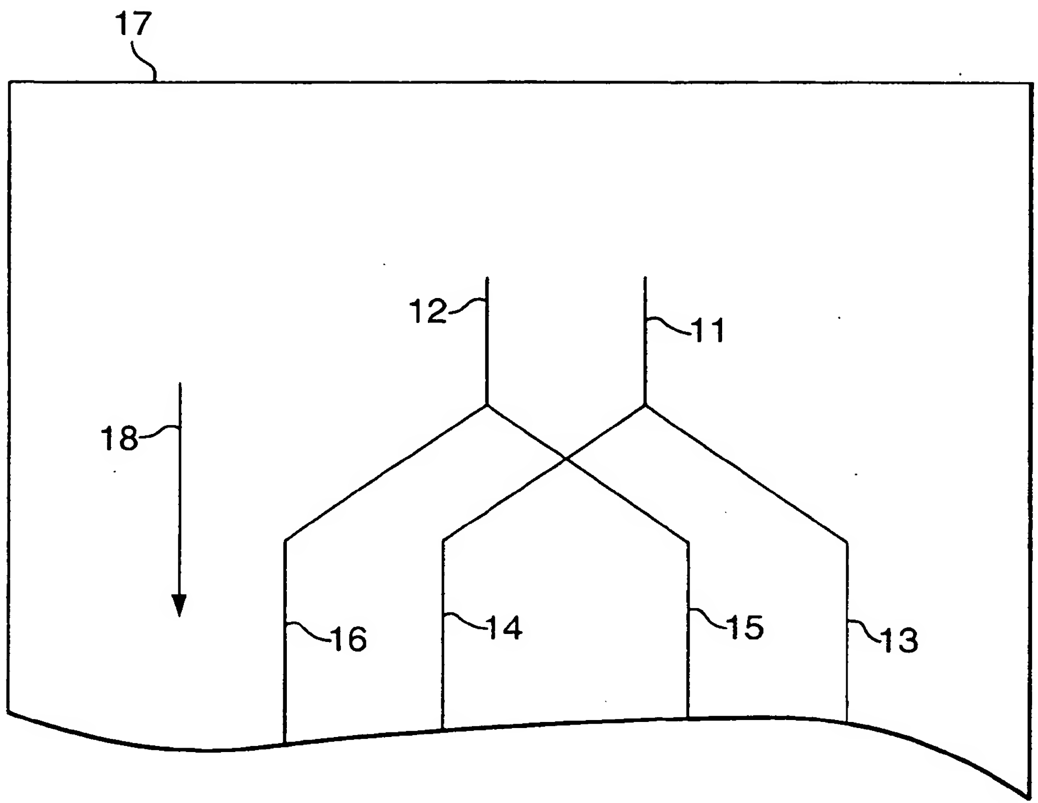


Fig.2.

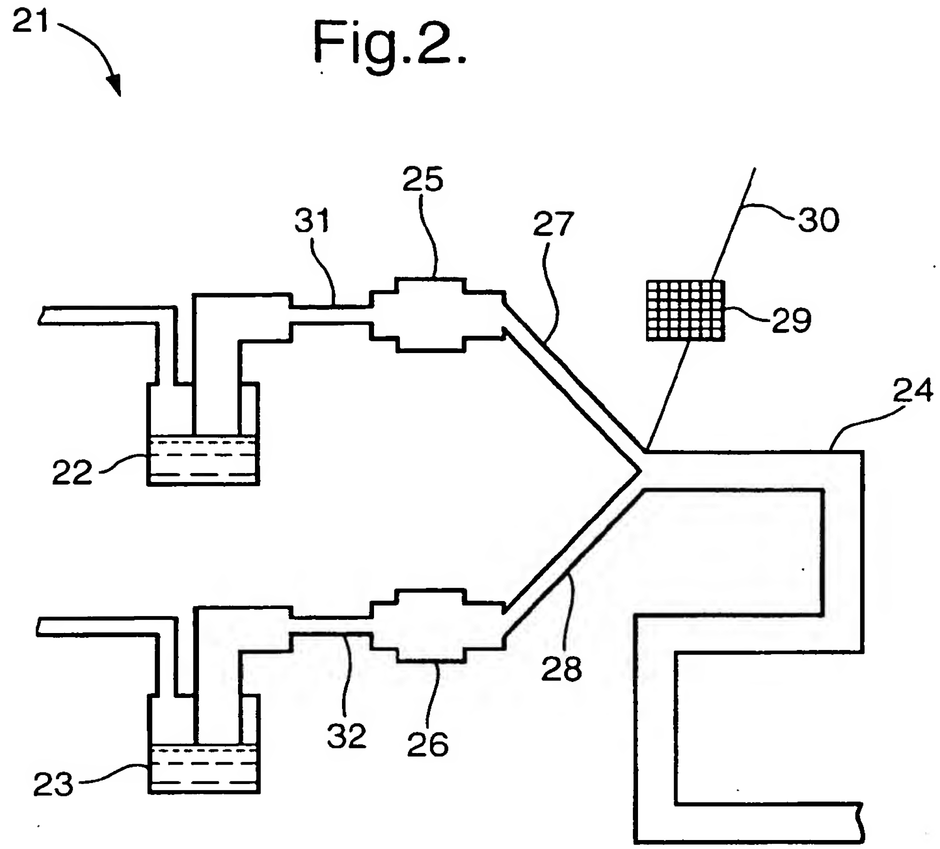


Fig.3.

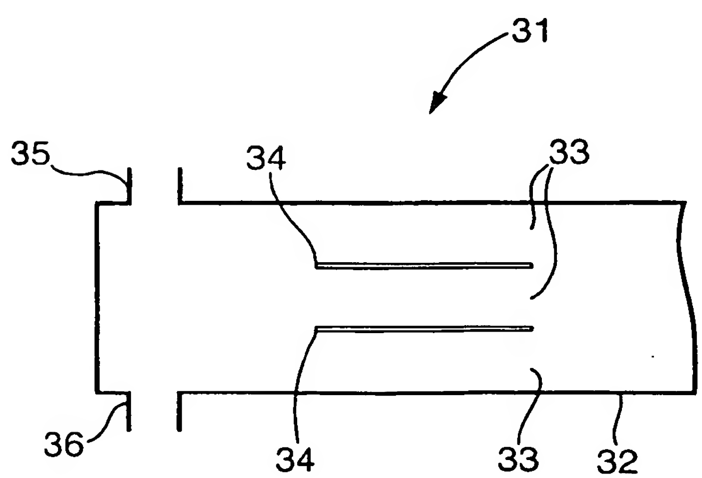


Fig.4.

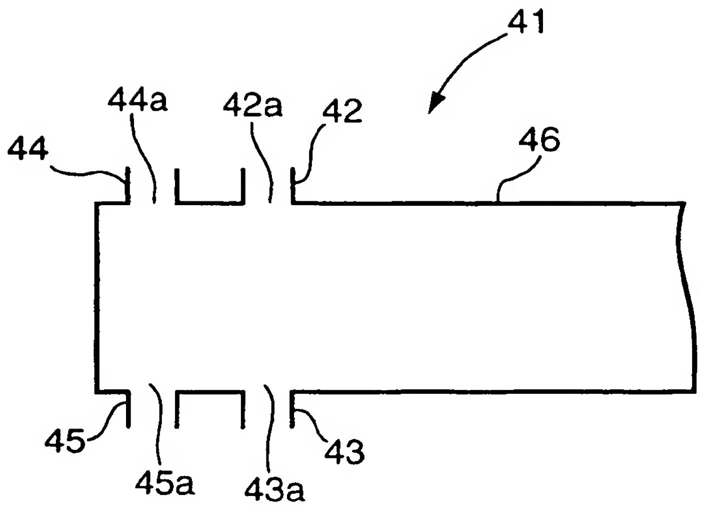


Fig.5.

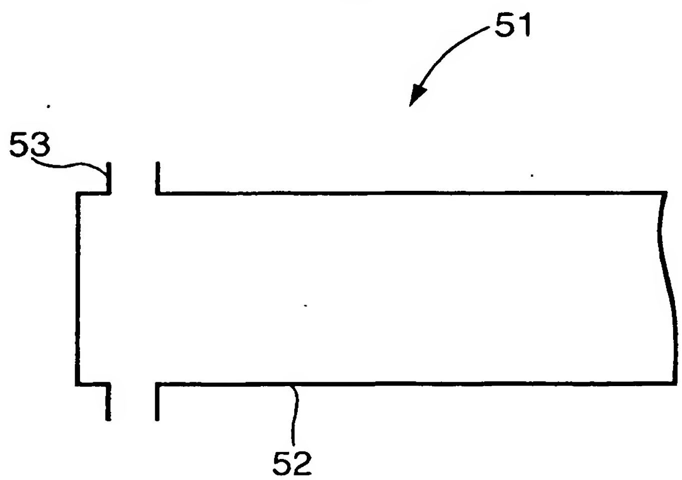


Fig.6.

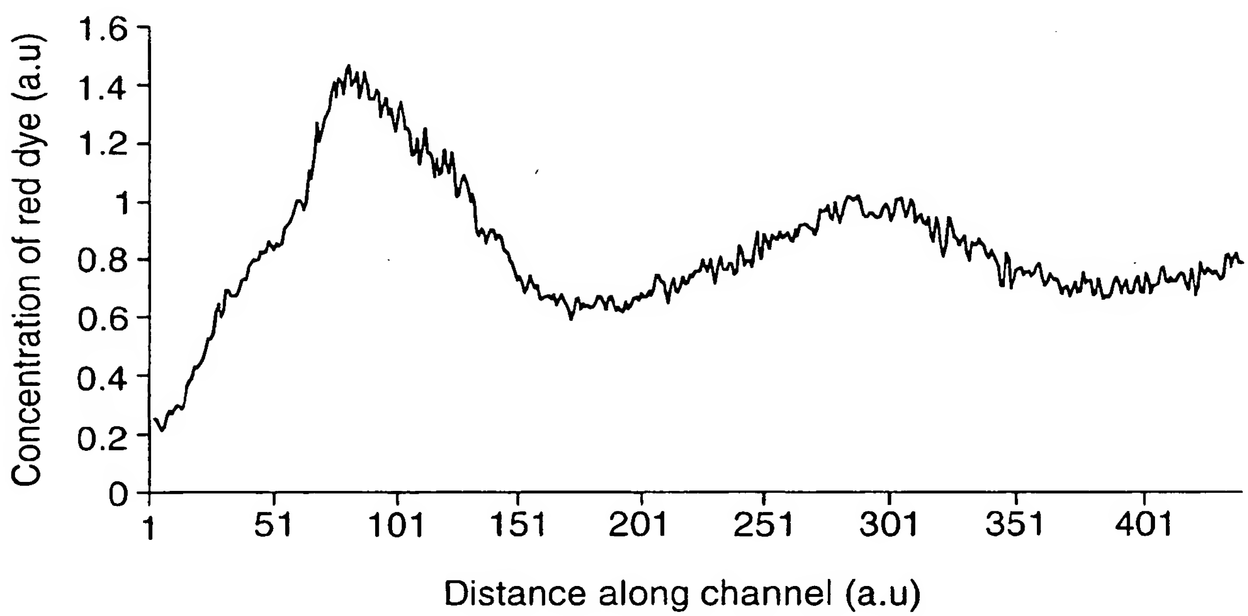

Concentration of red dye (a.u)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1
51
101
151
201
251
301
351
401
Distance along channel (a.u)

Fig.7(a).

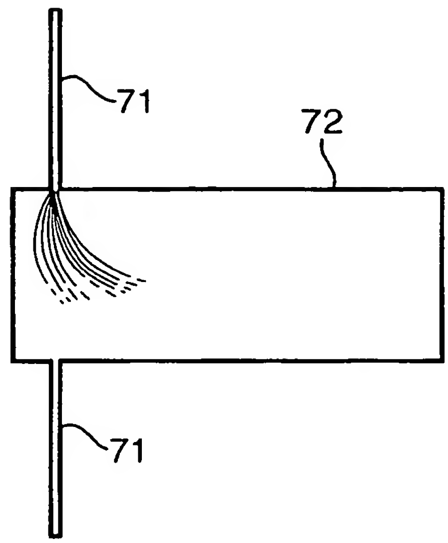
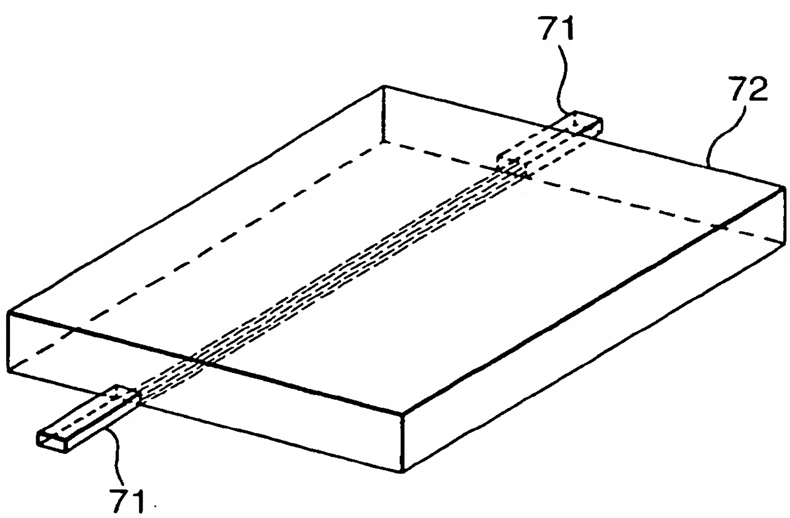


Fig.7(b).



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 02/00545

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01F13/00 B01F5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01F B01J G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	A. DESHMUKH: "SOLID STATE SENSORS AND ACTUATORS WORKSHOP, CROWNE PLAZA RESORT, HILTON HEAD, SOUTH CAROLINA, USA" 4 June 2000 (2000-06-04) XP008001735 cited in the application page 73 -page 76	1-11
X,P	GB 2 355 414 A (UNIV SHEFFIELD) 25 April 2001 (2001-04-25) cited in the application page 2, line 8 - line 27 page 5, line 24 - line 32; claims 1,2; figures 1,3,4,7A,7B	1-5,8-11
X,P	WO 01 93997 A (UNIV CALIFORNIA) 13 December 2001 (2001-12-13) the whole document	1-14

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 April 2002	17/05/2002

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inte   onal Application No
PCT/GB 02/00545

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 150 119 A (CHOW ANDREA W ET AL) 21 November 2000 (2000-11-21) cited in the application column 3, line 18 - line 41 column 4, line 4 - line 29 column 4, line 39 - line 55; figures 1,2	1-14
A	DE 196 11 270 A (GESIM GES FUER SILIZIUM MIKROS) 25 September 1997 (1997-09-25) cited in the application the whole document	1-14
A	GB 2 097 692 A (SHAW STEWART P D) 10 November 1982 (1982-11-10) the whole document	1-14

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte nal Application No
PCT/GB 02/00545

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
GB 2355414	A	25-04-2001	GB	2355543	A	25-04-2001
			AU	7807200	A	30-04-2001
			AU	7808400	A	30-04-2001
			AU	7808800	A	30-04-2001
			AU	7809100	A	30-04-2001
			WO	0129434	A1	26-04-2001
			WO	0129435	A1	26-04-2001
			WO	0128670	A1	26-04-2001
			WO	0128676	A1	26-04-2001
			GB	2355566	A	25-04-2001
			GB	2355567	A	25-04-2001
WO 0193997	A	13-12-2001	AU	6668001	A	17-12-2001
			WO	0193997	A1	13-12-2001
			US	2001055242	A1	27-12-2001
US 6150119	A	21-11-2000	AU	2853300	A	01-08-2000
			EP	1144674	A1	17-10-2001
			WO	0042212	A1	20-07-2000
DE 19611270	A	25-09-1997	DE	19611270	A1	25-09-1997
GB 2097692	A	10-11-1982	AU	1045983	A	04-06-1984
			EP	0124520	A1	14-11-1984
			WO	8402000	A1	24-05-1984
			JP	59501994	T	29-11-1984